# PATENT APPLICATION

"Express Mail" Mailing label number EV389959253US

Date of Deposit March 18, 2004

I hereby certify that this paper or fee is being deposited with the United States Postal Service "EXPRESS MAIL POST OFFICE TO ADDRESSEE" Service under 37 C.F.R. § 1.10 on the date indicated above and is addressed to the Mail Stop Patent Application, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Michael D. Beck
Name of person mailing Document or Fee

Michael D. Beck
Signature of person mailing Document or Fee


Applicant(s): Lance Middleton
490 Booth Hill Road
Trumbull, CT 06611

Scott Reed
25 Walnut Street
Monroe, CT 06468

Jared Walkenhorst
64 Longview Ave.
Fairfield, CT 06824


## SYSTEMS AND METHODS FOR MIXING FLUIDS


Michael D. Beck
Registration No. 32,722
Attorney Docket No. 1842-0028

Correspondence Address:
Maginot, Moore & Beck, LLP
Bank One Center/Tower
111 Monument Circle, Suite 3000
Indianapolis, Indiana 46204-5115
Telephone: (317)638-2922
Facsimile: (317)638-2139

# SYSTEMS AND METHODS FOR MIXING FLUIDS

## BACKGROUND OF THE INVENTION

This invention relates to systems and methods for mixing fluids, and particularly medical fluids. More specifically, the invention relates to improvements in syringe-to-syringe mixing systems.

Several systems have been developed for on-site mixing and dispensing of multi-part medical and dental compositions. One system uses dual-cartridge syringes with static mix tips. These systems are generally not adequate for mixing polymers with high mix ratios. A further drawback is that a considerable amount of material is wasted in the mix tip, which may not be problematic for low cost fluid compounds but is potentially prohibitive for expensive materials, such as an injectable disc nucleus material.

Another known system, known as continuous flow systems, uses an electromechanical apparatus that drives a mix tip for controlled mixing of the fluids. Continuous flow systems are best suited for "assembly line" production and are excessive and too expensive for mixing single batches of fluid compounds.

A system that is very compatible for mixing small batches includes two medical syringes connected by an adapter so that fluids can be pushed back and forth between the syringes. One such prior system is depicted in **FIGS. 1** and **2**. Two syringes **10** are coupled by an adapter **17**. The syringes can include Luer fittings **11** with similar fittings defined on the adapter. The adapter includes a uniform passageway **18** that allows flow of fluid from one syringe to the other as the plungers **15** are alternately depressed.

Syringe-to-syringe adapters like the adapter **17** have been used to couple a large reservoir syringe with a small dose syringe to simply transfer fluid from one to the other. These adapters have also been used to sequentially couple different syringes to a single syringe, each of the different syringes carrying a different fluid, or in some cases a granular compound to mix with the fluid in the

single syringe. In some cases, the two syringes contain different fluids that must be thoroughly mixed. This mixing occurs by alternately depressing the plungers **15** of the opposing syringes **10** so that the fluids flow back and forth through the adapter. Once the fluid transfer or mixing is complete, the syringes are uncoupled and one or both of the syringes can be used as an applicator or injection device.

For many types of fluids and fluid compounds, this mixing approach is sufficient. For instance, many emulsions are prepared through syringe-to-syringe mixing. In these prior devices, the constant diameter passageway **18** in the adapter **17** allows full uniform flow of the fluid through the adapter, and the resultant mixture is complete enough for the particular medical application. One drawback of these prior systems is that they require relatively high plunger forces when mixing viscous fluids, which can lead to user fatigue. Another problem is that it is time consuming to achieve uniform distribution of micro-droplets within a fluid mixture.

Furthermore, in certain medical applications, the degree of mixing that can be accomplished with prior adapters, such as the adapter **17**, is less than optimum. This problem manifests itself where high mix ratios are involved. For instance, certain injectable disc nucleus (IDN) compositions can have mix ratios between two constituents (i.e., polymer and cross-linker) greater than 10:1, and even greater than 100:1. The entire composition fails if the lower concentration constituent (such as the cross-linker in the case of an IDN) is not fully mixed within the other constituent (the polymer).

This mixing problem is also critical where the fluids combine to form a curable composition. In this case, as the different fluids are mixed they begin to cure, congeal or harden. For some materials, the curing time is sufficiently long so that the mixture can be cycled back and forth between the syringes enough times to ensure complete mixing of the constituents. For instance, many bone cements can be mixed using these types of prior devices.

However, the time necessary to achieve complete mixing is prohibitive for some curable materials that cure relatively quickly. If these types of materials are not dispensed in a timely manner, the mixture is worthless. For example, certain chemical compositions have been developed for the replacement of body tissues. One type of composition, known as hydrogels, is formed by mixing a polymer with a cross-linker. The resulting mixture starts to cure immediately when the constituents come into contact. For some hydrogels, the curing time is under two minutes. In these cases, it is imperative that the fluid mixing occur as quickly and completely as possible so that the surgeon has enough time remaining to inject the hydrogel at the surgical site.

The short curing times essentially prohibit mixing the constituents in any system other than a system that permits immediate injection of the mixture. In other words, syringe-to-syringe mixing is the most viable alternative for fluid compounds having short curing times.

Consequently, there is a need for a syringe-to-syringe system that yields complete mixing in mixing conditions that include one or more of the following parameters:

High mix ratios (e.g., much greater than 10:1);

Immiscible fluids;

Rapidly curing polymers; and

High viscosity fluids.

## Summary of the Invention

The present invention provides a syringe-to-syringe mixing apparatus that addresses these unresolved needs. In one embodiment, the mixing apparatus comprises an elongated body defining a passageway therethrough and configured at its opposite ends to engage a respective syringe thereat. The passageway communicates with the interior volume of each syringe so that fluid in each syringe can pass back and forth therebetween. In one feature of the invention, the mixing apparatus includes a flow modifying element disposed in the passageway that is configured to modify the flow of a fluid passing therethrough from syringe to syringe. The flow modifying element is configured to modify the fluid flow by increasing the flow velocity, disrupting the fluid flow or introducing turbulence.

In one preferred embodiment the flow modifying element is integrally formed in the body. In certain embodiments, the passageway defines a first flow area and the flow modifying element includes a restriction configured to increase the flow velocity therethrough, in which the restriction defines a second flow area less than the first flow area. In a specific embodiment, the first flow area is about five times greater than the second flow area.

The restriction assumes a variety of forms effective to disrupt the fluid flow and promote complete fluid mixing. For instance, the passageway and the restriction are substantially cylindrical in one embodiment, with the restriction constituting a nozzle. In other embodiments, the restriction is in the form of a slit, a multi-lobed opening, or a plurality of nozzles communicating between end portions of the passageway. In a further embodiment, the passageway includes a first portion adjacent one end of the passageway and a second portion adjacent the opposite end of the passageway, the first and second portions having longitudinal axes offset from each other. The restriction is then defined by an intersection between the first and second portions of the passageway.

In another aspect of certain embodiments of the invention, the body of the syringe-to-syringe mixing apparatus defines a mixing chamber between the flow

modifying element and at least one of the opposite ends of the passageway. The passageway can be configured to receive a portion of the syringe tip therein, with the mixing chamber defined between the flow modifying element and the syringe tip when the tip is received within the passageway.

In some embodiments of the invention, the flow modifying element includes at least two nozzles in the passageway, each configured to increase the flow velocity therethrough. The body defines an intermediate mixing chamber between successive ones of the at least two nozzles. The intermediate mixing chamber defines a first flow area and each of the at least two nozzles defines a second flow area less than the first flow area.

In yet another aspect of the invention, the flow modifying element includes at least two baffles forming a serpentine flow path through the passageway. The flow modifying element may also include a plurality of pins traversing the passageway to disrupt the fluid flow through the mixing apparatus.

In some applications of the invention it is desirable to add a small quantity of an additional constituent to the fluid being mixed between the opposing syringes. Consequently, the invention contemplates means for introducing this constituent into the fluid flowing through the mixing apparatus. In one embodiment of the invention, the mixing apparatus body defines an orifice in communication with the passageway between the opposite ends thereof. The mixing apparatus is configured to receive a device for injecting the constituent through the orifice, such as a syringe.

In one feature of this embodiment, the orifice is a sealed orifice. The apparatus can further comprise a valve covering the orifice to prevent flow of the constituent therethrough. In one embodiment, the valve is a septum covering the orifice. The septum is adapted to be penetrated by a fluid introduction component, such as a syringe needle. In one specific embodiment, the septum is formed of a self sealing material, such as SILASTIC®, that seals around a needle when pierced and resiliently closes when the needle is removed. In another specific embodiment the septum includes a slit that is resiliently sealed

by the septum material but can open upon pressure from the fluid introduction component.

The mixing apparatus is configured to accept the tips of opposing syringes. Thus, the passageway of the mixing apparatus body can be configured for a fluid-tight press-fit engagement with the tips of the syringes. The body can also include fittings at its opposite ends that are configured to engage the syringe. For instance, the fittings can be Luer fittings to engage complementary fittings on the syringes.

The present invention further contemplates an improvement to a syringe-to-syringe mixing apparatus comprising a nozzle element disposed within the tip of a syringe. The nozzle element defines a passageway therethrough in communication with the interior volume of the syringe and includes a restriction in at least one end of the nozzle element adjacent the interior volume of the syringe. The restriction is configured to increase the flow velocity therethrough. In one embodiment, restriction includes at least a portion of the passageway having a flow area that decreases toward the interior volume of the syringe.

In certain embodiments, the nozzle element is an insert configured to be mounted within the tip of the syringe. The insert includes a retaining flange at an opposite end of the nozzle element, wherein the retaining flange is configured to engage the end of the syringe tip. The insert can be configured to be inserted into the tip of the syringe through the interior volume of the syringe. In another embodiment, the nozzle element is integrally formed within the tip of the syringe.

The invention further provides in a syringe-to-syringe mixing system of the type having two syringes adapted to reciprocally pass fluid therebetween until mixed, a mixing apparatus comprising means for modifying the flow of fluid between the two syringes. This means is adapted to communicate with each of the two syringes and is preferably configured for disposition between the two syringes.

In one embodiment, this means for modifying the flow of fluid can include an elongated body, adapted at its ends to engage a corresponding one of the two syringes. The elongated body defines a fluid passageway in communication with the two syringes and a restriction within the passageway. The restriction can be in the form of a nozzle adapted to significantly increase the fluid flow velocity through the apparatus.

In another embodiment, the means modifying the flow of fluid is configured for disposition within one of the two syringes. In this embodiment, the means for modifying the flow of fluid can include a nozzle insert configured for engagement within the tip of one of the two syringes.

It is one object of the present invention to provide a syringe-to-syringe mixing system that efficiently mixes at least two constituents of a fluid composition. It is one particular object to provide a mixing system that can quickly and thoroughly mix the constituents of a composition that is "time sensitive", such as compositions that begin curing when mixed.

Another object is to provide a mixing system that can accept the introduction of small quantities of a constituent. A further object is to permit introduction of this constituent at any point in the mixing of the other constituents of the composition.

One benefit of the mixing apparatus of the present invention is that it can be used with traditional syringe-to-syringe mixing systems. Another benefit is that it provides complete and rapid mixing with minimal effort on the part of medical personnel. A further benefit of the present invention is that it is ideally suited for mixing self-curing compositions, or compositions that begin curing once the constituents come in contact with each other in appropriate ratios.

Other objects and benefits of the invention will become apparent upon consideration of the following written description, taken together with the accompanying figures.

## DESCRIPTION OF THE FIGURES

**FIG. 1** is perspective view of a syringe-to-syringe mixing system of the prior art.

**FIG. 2** is a cross-sectional view of the adapter used in the mixing system shown in **FIG. 1**.

**FIG. 3** is a side cross-sectional view of a syringe-to-syringe mixing system in accordance with one embodiment of the present invention.

**FIG. 4** is a side cross-sectional view of a mixing apparatus for use in the mixing system shown in **FIG. 3**.

**FIG. 5** is a side cross-sectional view of an alternative mixing apparatus for use in the mixing system shown in **FIG. 3**.

**FIG. 6** is a side cross-sectional view of yet another alternative mixing apparatus for use in the mixing system shown in **FIG. 3**.

**FIG. 7** is an end cross-sectional view of a further nozzle configuration for a mixing apparatus for use in the mixing system shown in **FIG. 3**, the cross-sectional view being taken along line A-A in **FIG. 3**.

**FIG. 8** is an end cross-sectional view of a still further nozzle configuration for a mixing apparatus for use in the mixing system shown in **FIG. 3**, the cross-sectional view being taken along line A-A in **FIG. 3**.

**FIG. 9a** is a side cross-sectional view of yet another alternative mixing apparatus for use in the mixing system shown in **FIG. 3**.

**FIG. 9b** is an end cross-sectional view of the nozzle configuration for a mixing apparatus shown in **FIG. 9a**, the cross-sectional view being taken along line B-B in **FIG. 9a**.

**FIGS. 10 - 13** are side cross-sectional views of other alternative mixing apparatus for use in the mixing system shown in **FIG. 3**.

**FIG. 14** is an exploded perspective view of a mixing apparatus in accordance with a further embodiment of the invention.

**FIG. 15** is side cross-sectional view of the mixing apparatus shown in **FIG. 14** in its assembled configuration.

**FIG. 16a** is representation of fluid flow patterns into a syringe using prior syringe-to-syringe mixing techniques.

**FIG. 16b** is a comparative representation of fluid flow patters into a syringe using the syringe-to-syringe mixing apparatus of **FIGS. 14-15**.

**FIG. 17** is a side cross-sectional view of a syringe modified in accordance with one embodiment of the present invention.

**FIG. 18** is a partial cross-sectional view of a nozzle insert being positioned within the tip of a syringe to form the mixing apparatus shown in **FIGS. 14-15**.

**FIG. 19** is a side cross-sectional view of a mixing apparatus of still another embodiment of the invention.

**FIG. 20** is a side cross-sectional view of a mixing apparatus with a one piece septum.

## DESCRIPTION OF THE PREFERRED EMBODIMENTS

For the purposes of promoting an understanding of the principles of the invention, reference will now be made to the embodiments illustrated in the drawings and described in the following written specification. It is understood that no limitation to the scope of the invention is thereby intended. It is further understood that the present invention includes any alterations and modifications to the illustrated embodiments and includes further applications of the principles of the invention as would normally occur to one skilled in the art to which this invention pertains.

The present invention contemplates a mixing apparatus for use with a pair of syringes, such as the syringes **10** shown in **FIG. 1**. The mixing apparatus can be configured to mate with any syringes, such as by a press-fit engagement with the syringe tip, by Luer connection or other suitable means. As shown in **FIG. 3**, the syringe **10** can include a Luer fitting **11** with a fluid dispensing tip **14** extending concentrically therethrough. In accordance with one embodiment of the invention, a mixing apparatus **20** is connected between the two syringes. The apparatus **20** includes an elongated body **22** that defines a passageway **23** therethrough. The passageway **23** extends through fittings **28** at the opposite ends of the body. The fittings are configured to mate with either or both of the syringe Luer fitting **11** or tip **14**. Preferably, the fittings **28** are configured to form a fluid tight engagement between the passageway **23** of the mixing apparatus and the dispensing tip **14** of the syringe. The exterior of the elongated body **22** can be configured to define a gripping surface to facilitate engagement of the apparatus to the syringes.

The passageway **23** is initially sized to receive the syringe tip **14** at the opposite ends of the mixing apparatus **20**. In accordance with one feature of the invention, a flow modifying element **25** is disposed within the passageway. The flow modifying element is configured to modify the flow of a fluid through the passageway, such as by increasing the flow velocity, disrupting the fluid flow or introducing turbulence. In accordance with the embodiment of the invention

shown in **FIG. 3**, the flow modifying element **25** includes a decrease in the size of the passageway to a nozzle **26** within the body **22**. The term "nozzle" as used herein refers to structure that produces an increase in the velocity of fluid passing through the nozzle. In one particular embodiment, the passageway and nozzle have circular cross-sections, with the passageway gradually decreasing in diameter from the fittings **28** to the nozzle **26**. The flow modifying element **25** or nozzle **26** can be integrally formed in the body **22** or can be a separate component that is inserted and fixed within the passageway **23**.

The engagement between the syringe tip **14** and the fittings **28** of the mixing apparatus is configured to provide a mixing chamber **24** on each side of the nozzle **26**. The nozzle operates to increase the flow velocity of fluid passing therethrough. The increase in cross-sectional area from the nozzle to the mixing chambers **24** preserves the greater fluid shear rates generated by the nozzle. A significant amount of fluid mixing occurs in the mixing chambers **24**, but fluid mixing continues as the fluid is pushed from one syringe to the other.

In accordance with one feature of this embodiment, the length of the nozzle is comparatively short relative to the length of the mixing chambers **24** and passageway **23**. Keeping the length of the nozzle to a minimum reduces the force that must be applied to drive the fluid through the nozzle. In a specific embodiment, the length of the nozzle is about twice its effective diameter. The nozzle **26** in this embodiment has an effective diameter of about 0.05 inches, and a length of about 0.1 inches. The passageway **23** has an effective diameter that is about five times greater than the nozzle diameter.

Other embodiments of the mixing apparatus include different nozzle configurations for the flow modifying element that do not employ as gradual a change as the embodiment of **FIG. 3.** For example, the embodiments illustrated in **FIGS. 4-8** provide a more abrupt change in flow diameter. This abrupt change may be less efficient from a thrust perspective, but provides an efficient nozzle with non-laminar flow from a mixing perspective.

The mixing apparatus **30** shown in **FIG. 4** includes a body **31** that defines a passageway **32** therethrough. A restriction **33** in the interior of the body creates a nozzle opening **34** in the passageway **32**. This nozzle constriction serves the same purpose as the nozzle **26** described above. The embodiment shown in **FIG. 5** is similar to that of **FIG. 4**, except that the length of the nozzle restriction has been increased. Thus, the mixing apparatus **35** of **FIG. 5** includes a body **36** that defines the passageway **37** and the restriction **38**. The resulting nozzle **39** extends over a significant portion of the length of the apparatus **35**.

In the embodiment shown in **FIG. 6**, the nozzle is formed by the intersection of offset passageways. The mixing apparatus **40** includes a body **41** that defines two passageways **42, 43** from either end of the body. The passageways are offset but intersect at their inner extent. This intersection forms the nozzle **44**. It should be understood with respect to each of the embodiments of **FIGS. 4-6** that the passageways are configured like the passageway **23** to form a fluid-tight engagement with the syringe tip **14** and to provide a mixing chamber, such as the chamber **24**, adjacent each syringe tip.

Variations in the configuration of the nozzle **26** (**FIG. 3**) are further illustrated in **FIGS. 7** and **8**. As indicated above, the nozzle **26** is circular in cross-section. As shown in **FIG. 7**, the nozzle **26'** within a body **22'** can be slit-shaped. The height of the slit **26'** can be less than the effective diameter of the nozzle **26**, although the effective area can be the same between the two nozzle variations. As a further alternative, a nozzle **26"** can be multi-lobed, as depicted in **FIG. 8**. Each lobe of the nozzle can act as a miniature nozzle to locally increase the fluid flow relative to the central portion of the lobed nozzle. Thus, this approach can produce a fluid velocity gradient that can enhance mixing.

In a variation of the lobed nozzle concept, the flow modifying element for a mixing apparatus **45** of **FIGS. 9a-b** includes a plurality of miniature nozzles **48** defined in the body **46** at the interior of the passageway **47**. These nozzles **48** produce several fluid "jets" that disperse within the mixing chambers to produce turbulent mixing.

In another approach, the flow modifying element includes a series of baffles interposed in the fluid flow path between the syringes. For example, as depicted in **FIG. 10**, the body **51** of a mixing apparatus **50** defines a passageway **52** therethrough that is interrupted by a series of restrictions or nozzles **53**. The nozzles **53** form a series of intermediate chambers **54** so that the fluid is alternately restricted and expanded as it flows through the apparatus. As depicted in **FIG. 10**, the restrictions and intermediate chambers are uniform and cylindrical. Alternatively, the nozzles **53** and intermediate chambers **54** can form a spiral volume through the body **51**.

The mixing apparatus **60** shown in **FIG. 11** includes a series of alternating restrictions **63** that constitute the flow modifying element. The restrictions form a serpentine path for the fluid flow through the passageway **62** defined in the body **61**. The restrictions **63** also define a reduced area **64** that operates as a nozzle to accelerate the fluid velocity. The restrictions **63** can take on a variety of forms, such as a wall across a chord of the circular area of the passageway **62**.

The embodiments shown in **FIGS. 12** and **13** rely upon flow modifying elements interposed in the passageway that disrupt the fluid flow. The mixing apparatus **65** shown in **FIG. 12** includes a body **66** that defines a passageway **67** therethrough. The passageway may have a uniform cross-section throughout. The body further defines a plurality of bores **68** that at least open into the passageway **67**, but preferably extend entirely through the body. The bores are oriented transverse to the length of the passageway, preferably, but not necessarily, at right angles to the passageway. The bores **68** support pins **69** that extend through the passageway **67**. As illustrated in **FIG. 12**, the pins can be disposed at various angular orientations about the axis of the passageway. The pins **69** are preferably press-fit within the bores **68** to form a fluid-tight engagement. The pins may have an effective width within the fluid flow path that is significantly smaller than the effective diameter of the path. In a specific embodiment, the pins have a width of about 1/10$^{th}$ the flow path diameter.

The pins have an effective width that is sufficient to disrupt the fluid flow through the passageway, but not so large that they greatly increase the flow resistance of the mixing apparatus. The pins generate eddies downstream of the pins with enough flow velocity through the passageway, which help mix the fluid constituents. Although the embodiment illustrated in **FIG. 12** only includes five pins, greater numbers at smaller angular increments are contemplated.

The mixing apparatus **70** shown in **FIG. 13** employs a similar concept. The body **71** of the apparatus supports a brush array **73** within the passageway **72**. The brush array **73** includes small diameters pins or needles, but relies upon a large number across the flow path to produce desirable mixing characteristics.

In using the apparatuses shown in **FIGS. 3-13**, each syringe **10** contains one of the two fluid constituents. The syringes are at most only half-filled with their respective fluids. Where the mixing ratios are high, the volume of fluid in one syringe may be significantly greater than the volume in the other. Once air is purged from each syringe, any one of the mixing apparatuses in **FIGS. 3-13** can be engaged to one of the syringes. The plunger is depressed to push fluid into the passageway of the mixing apparatus until a meniscus is formed at the open end of the passageway. The second syringe can then be engaged to the mixing apparatus. In addition, a device can be provided for injecting another constituent in small quantities, as described in more detail herein.

Fluid mixing occurs by alternately depressing the plungers **15** of the two syringes. The speed and number of alternating plunger movement depends upon the type of material being mixed. For some polymer compositions, ten cycles in ten seconds is sufficient for complete mixing of the fluid constituents.

The mixing adapters depicted in the figures are all "in line", meaning that the longitudinal axes of the syringes and the mixing apparatus are coincident. While this arrangement is believed to be optimum, it is possible to configure the mixing apparatuses to mate with non-aligned syringes. With this alternative configuration, at least a portion of at least one of the mixing chambers will be configured to change the direction of the fluid flow into the non-aligned syringe.

In the embodiments of the invention illustrated in **FIGS. 3-13**, the fluid mixing occurs primarily in the body of the mixing apparatuses. In these apparatuses **20, 30, 35, 40, 45, 50, 60, 65** and **70**, mixing chambers **24** are defined within the central passageway as the volume between the restriction or nozzle and the tip **14** of the syringe. Fluid mixing occurs throughout the system, but the most intense fluid mixing occurs in these mixing chambers due to their proximity to the flow modifying element.

The present invention contemplates an alternative embodiment in which most of the fluid mixing occurs in the syringes themselves. In one exemplary embodiment shown in **FIGS. 14-15**, a mixing apparatus **80** is coupled between two syringes **10**, which can be conventional syringes as discussed above. The mixing apparatus **80** includes a body **82** that defines a passageway **83** therethrough. The fittings **84** shown in **FIG. 14** at the ends of the body can be similar to the fittings **28** of the embodiment discussed above with reference to **FIG. 3**. Alternatively, the fittings can be configured for a press-fit only, such as the fittings **84'** shown in **FIG. 15**.

In accordance with this alternative embodiment, a nozzle insert **90** is inserted into the tip **14** of at least one of the syringes **10**. As best seen in **FIG. 15**, the nozzle insert **90** is formed by an elongated tubular body **91** that is configured for a fluid-tight engagement within the syringe tip **14**, such as by a press-fit. In certain embodiments, the insert **90** includes a retaining flange and groove feature **92** that interlocks with a circumferential ridge **14a** typically formed on the syringe tip **14**. This interlocking engagement can be sufficient to hold the nozzle insert **90** within the tip **14**, even where the insert has only a close running fit (rather than a press fit) within the syringe tip.

Again as seen in **FIG. 15**, the nozzle insert **90** defines a passageway **93** therethrough. This passageway includes a restriction **94** at the inner end of the nozzle insert – i.e., immediately adjacent the interior volume of the syringe when the insert is positioned within the syringe tip **14**. This restriction **94** serves to increase the flow velocity as the fluid mixture enters the syringe **10a**. In the

preferred embodiment, the restriction **94** defines a circular flow area. However, the restriction can assume other configurations, such as the configurations depicted in **FIGS. 7, 8** and **9b**.

The benefits of this nozzle insert **90** can be discerned by the comparison in **FIGS. 16a-b**. The depiction in **FIG. 16a** represents fluid flow through the standard syringe tip **14** directly into the syringe interior volume. As the plunger **15** is withdrawn, the fluid exits the tip **14** in a fluid stream **115** having a velocity V1. As the plunger moves farther from the tip **14**, a region **116** of poor fluid circulation arises as the fluid stream **115** decays into laminar flow behind the plunger.

In contrast, **FIG. 16b** depicts the fluid flow through the nozzle insert **90**. The fluid stream **118** discharged from the insert **90** has a much higher flow velocity V2 than the standard configuration in **FIG. 16a**. This greater flow velocity means that the high velocity fluid stream extends farther into the syringe **10a** even as the plunger **15** is withdrawn. In one embodiment, the velocity V2 is five times greater than the velocity V1 achieved in a conventional syringe-to-syringe mixing system. Ideally, the size of the restriction **94** in the nozzle insert **90** is calibrated to that the fluid stream **118** does not deteriorate into laminar flow until the plunger has reached its maximum withdrawal, if at all. The high velocity fluid stream **118** passes through a virtual "wall" of stationary or slower moving fluid **119** around the stream **118**. This results in high shear rates, which ultimately results in greater mixing than can be accomplished with the conventional syringe-to-syringe system depicted in **FIG. 16a**.

In an alternative approach, the restriction can be integrated into the syringe tip itself, as illustrated in **FIG. 17**. A syringe **120** can include a tip **121** that defines a fluid passageway **122**. The interior end of the passageway defines a nozzle **123** to produce the high velocity jet flow **124** contemplated in **FIG. 16b**. In the preferred embodiment, the passageway **122** is tapered toward the nozzle **123** to gradual restrict the fluid flow being drawn into the syringe **120**. This

modified syringe tip **121** achieves the same beneficial fluid flow characteristics discussed above relative to the nozzle insert **90**.

While the preferred embodiment contemplates a restriction **94** that produces an increase in flow velocity, another alternative is to disrupt the fluid flow into the syringe. Thus, the restriction can be replaced by the flow modifying elements depicted in **FIGS. 12-13**. Introduction of the pins **69** or needles **73** disrupts the fluid flow, producing turbulence of eddies that may improve fluid mixing within the syringe.

Returning to **FIGS. 14** and **15**, a further feature of the invention is the provision of a septum for injection of a fluid constituent into the mixing apparatus **80**. In particular, the body **82** defines a septum bore **100** that intersects the passageway **83** through the body. The bore terminates in a small diameter orifice **101** that is sized to receive a hypodermic needle. The orifice **101** is covered by a septum **103** that is formed of a self-sealing material. In particular, the septum **103** is configured to be penetrated by a needle **111** attached to a syringe **110** carrying an additional fluid constituent. A set screw **105** is threaded into the septum bore **100** to press and retain the septum within the bore and keep it taut for penetration by the needle **111**. The septum can be formed of a conventional self-sealing material, such as SILASTIC®, or may include a slit therethrough as is known in the art.

The septum orifice **101** provides means for introducing an additional fluid into a mixture, where one or more other fluids are contained within the syringes **10, 10a**. In addition, the orifice **101** supplies an avenue for the introduction of a low ratio fluid constituent. For instance, where the mix ratio is 100:1 and above, the volume of one constituent is extremely small compared to the volume of the constituent contained in one of the syringes **10**. Carrying this low ratio fluid in one of the syringes **10** may not result in a complete mixing of the two fluids. Thus, the introduction of the low ratio fluid directly into the fluid flow passing through the mixing apparatus **80** ensures that the low ratio fluid will be entrained within the higher volume fluid.

Although the septum feature is depicted in combination with the nozzle insert, the septum can be integrated into any of the mixing apparatuses shown in **FIGS. 3-13**. In that case, the septum orifice **101** can intersect the nozzle (e.g., the nozzle **26**) or one of both of the mixing chambers **24** or the syringe **10**.

The septum provides a ready interface for needle injection of a fluid into the mixing stream. Alternatively, the septum bore **100** can be used as a reservoir to hold a fluid constituent. The orifice **101** can be sized and arranged within the body **82** to act as a venturi orifice. As fluid flows past the orifice **101**, the reduced pressure will draw fluid from the bore/reservoir **100** to mix with the fluid passing through the passageway **83**. Optimally, where the orifice serves as a venturi opening, the orifice **101** is positioned at a narrowing in the passageway, such as at the nozzle **26** of the apparatus **20** shown in **FIG. 3**, so that the increased flow velocity will rapidly draw the fluid into the flow.

In one application of the mixing apparatus **80** shown in **FIGS. 14-15**, the syringes **10**, **10a** are 5ml syringes. Syringe **10** is filled with 4.5 ml of a polymer used to form an IDN composition. The mixing apparatus **80** is engaged to the syringe **10a** and air within the syringe and apparatus is purged.

Next, the plunger **14** is removed from the other syringe **10a** and the nozzle insert **90** is mounted on an insertion tool **126**. As depicted in **FIG. 18**, the insertion tool is used to push the nozzle insert **90** into the syringe tip **14** from the inside of the syringe. This approach is particularly necessary where the interior of the tip is inwardly tapered away from the barrel of the syringe. The insert is pushed into the tip until the retaining flange and groove **92** snap around the ridge **14a** at the interior of the distal end of the tip. The plunger **14** is then reinserted into the syringe and the second syringe **10a** is attached to the mixing apparatus **80**

About 2 ml of the polymer in the first syringe **10** is transferred into the second syringe **10a** and that syringe is detached from the mixing apparatus. Air is again purged from both syringes with care given to ensuring that a positive meniscus is formed at the tip of the second syringe **10a** and at the open end of

the mixing apparatus. The assembly is completed by re-attaching the second syringe to the mixing apparatus.

The polymer in the second syringe **10a** is then shifted back to the first syringe **10** and the filled assembly is placed aside until the final IDN composition is needed for introduction into the patient. When that point arrives, a third syringe **110** loaded with a cross-linker is provided. The needle **111** punctures the septum **103** and the full pre-measured quantity of cross-linker is injected into the mixing apparatus **80**. This solution is then mixed by cycling the syringe plungers **14** back and forth for ten cycles in 7-10 seconds, ending with the entire volume in the first syringe **10**. The surgeon then has a limited amount of time to inject the mixed IDN composition into the patient's disc, under 1½ minutes for certain compositions. The first syringe is detached from the mixing apparatus and an injection needle mounted to the syringe to accomplish the disc injection.

An alternative mixing apparatus **130** is illustrated in **FIG. 19**. A body **132** defines a passageway **133**, a septum bore **135** and an orifice **137**. A septum **139** is contained within the bore by a set screw **141**. The apparatus **130** includes a nozzle insert **145** that is mounted within the tip **14** of the two syringes **10**. The nozzle insert includes a head **147** that is trapped within the body **132**, closing the passageway **133** to define a chamber **134**. The nozzle inserts **145** are much longer than the insert **90** of **FIGS. 14-15**, but include the same restriction feature **148**. Unlike the nozzle insert **90**, the inserts **145** are configured to be inserted into the syringe tips **14** from the outside of the syringe, rather than from the inside, as described above.

In this embodiment, the apparatus **130** includes a pair of connectors **150** that connect the body **132** to the two syringes and that traps the head **147** of each nozzle insert **145** within the body. Each connector includes a threaded fitting that mates with threads defined in the open ends of the passageway **133**. As the connector **150** is threaded into the passageway it clamps the head **147** of the insert **145** within the body. The connectors **150** also include a Luer fitting **154** for mating with the Luer fitting **11** of each syringe. The Luer fittings **154** define a

channel **156** for receiving the syringe tip **14** therein. The connectors **150** may include a thumb wheel **158** to facilitate threading the fittings **152, 154** into their respective mating fittings.

In an alternative configuration, the syringe tip can be provided with external threads to engage the internal threads in the passageway **133** of the body **132**. With this alternative, the body can be mounted on the tip **14** without the connector **150**, and can directly trap the head **147** of the insert **145** between the body and the end of the syringe tip.

The mixing apparatus **130** demonstrates that a nozzle insert can be provided in both syringes, rather than in one syringe only. The mixing apparatus also contemplates a longer fluid flow path between the syringes than most of the prior embodiments. This longer flow path can provide beneficial mixing characteristics for certain fluid compositions.

In a further modification, a one-piece septum component **180** can be engaged within a mixing apparatus **170**, as shown in **FIG. 20**. The mixing apparatus **170** of **FIG. 20** can be configured like the apparatus **80** shown in **FIG. 15**. In particular, the apparatus defines a flow passageway **171** that is intersected by a septum bore **172**. The bore **172** defines an orifice **174**, similar to the bore and orifice shown in **FIG. 15**.

In a modification from this prior embodiment, the septum bore **172** defines a septum seat **176** and an enlarged cavity **178**. The septum component **180** includes a septum portion **182** that bears against the septum seat **176** directly above the orifice **174**. The component **810** further includes an enlarged flange **186** that is sized to expand into the enlarged cavity **178** when the septum portion is seated on the septum seat. The septum component **180** is formed of a resiliently compressible material, such as SILASTIC®, so that the flange **186** can be compressed to squeeze through upper portion of the bore **172** and then resiliently expand outward into the cavity **178**. The flange is configured to hold the septum component **180** within the septum bore **172** and maintain a fluid-tight seal between the septum portion **182** and the septum seat **176**.

The septum component **180** defines an open bore **184** that terminates at the septum portion **182**. The bore **184** serves as a guide for a syringe, such as the syringe **110** depicted in **FIG. 15**. The septum material can be readily and sealingly penetrated by the needle **111** to accomplish injection of the additional constituent. The septum component **180** can include a handle **188** that can be manually grasped to insert and remove the component from the mixing apparatus **170**.

While the invention has been illustrated and described in detail in the drawings and foregoing description, the same should be considered as illustrative and not restrictive in character. It is understood that only the preferred embodiments have been presented and that all changes, modifications and further applications that come within the spirit of the invention are desired to be protected.

For example, the nozzle insert **90** can be combined with a mixing apparatus **20** or its variations shown in **FIGS. 4-13**. The body of any of the mixing apparatuses described above may also be provided with more than one septum orifice **101** to permit simultaneous introduction of two different fluids. As a further alternative, the septum set screw **105** can incorporate a fluid dispensing component, such as an integral syringe or a primer bulb that can be operated to push through the orifice. In certain applications, the septum **103** can be replaced with a valve element, such as a valve flap.

As described above, the syringe-to-syringe mixing systems are hand supported. Gripping elements can be added to the syringes to facilitate gripping of the syringes and manipulation of the syringe plungers. Alternatively, a fixture can be provided to support the syringes and/or mixing apparatus. Furthermore, while the illustrated embodiments contemplate manually operated syringes, the mixing apparatuses and nozzle inserts can also be used with powered fluid dispensing systems.

The principles of the present invention can also be employed to mix granular or particulate constituents with a fluid. In this instance, the granular

constituents can be contained in one syringe and the fluid constituent in the other. The nozzle insert can be engaged within the first syringe so that the "jet flow" will agitate the granular material as the fluid is injected.